

REMARKS/ARGUMENTS

Status of the Claims

Claims 143 to 146, 148 to 151, and 188 to 190 were previously presented and are currently pending in the application. Claims 143, 144, 146 and 150 are herein amended. Upon entry of the current amendment, claims 143 to 146, 148 to 151, and 188 to 190 will be pending for examination.

Claims 143, 144, and 150 stand objected to because of several alleged informalities which are addressed further below.

Claims 143-146, 148-151, and 188-190 stand rejected pursuant to the judicially created doctrine of obviousness type double patenting as being allegedly unpatentable over each of U.S. Patents Nos. 6,150,176 and 6,780,975.

Claims 143-146, 148-151, and 188-190 stand newly rejected on the ground of nonstatutory obviousness-type double patenting as being allegedly unpatentable over claims 1-13 and 17-26 of U.S. Patent No. 7,015,310.

Claims 143-146, 148-151 and 188-190 are rejected under 35 U.S.C. § 112, first paragraph, for an alleged lack of enablement

Amendments to the claims

Claims 143 and 144 have been amended in order to remove the parentheses from the recital of SEQ ID NO:2, to properly state the various substitutions at position 148 in the alternative, and to properly place the Markush groups in proper form, as requested by the examiner. Claims 143 and 144 are further amended in order to set forth a particular embodiment, wherein said functional engineered fluorescent protein has fluorescent emission in the visible spectrum. While there is no *in haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure (*see*, MPEP §2163 I(b) at 2100-175 of Rev. 6, September 2007). This subject matter is implicit in the descriptions. Support for the latter recital can be found *inter alia* throughout the specification and more particularly in the paragraph bridging page 62 line 26 which discusses *multicolor* reporting as a use of the subject proteins.

Claims 143, 144, and 146 have been amended to fix typographical errors made without deceptive intent, in which hyphens and commas were inadvertently inserted into the claims.

Accordingly, the Applicants believe the amendments to the claims add no new matter and respectfully request their entry.

Compliance with the sequence listing requirements of 37 CFR 1.821(a)(1) and (a)(2):

Applicants request entry of the paper copy of the substitute sequence listing submitted 9 April 2008 into the specification in adherence with 37 C.F.R. §§1.821 to 1.825. These amendments add no new matter. Accordingly, the Applicants respectfully request entry of the sequence listing and reconsideration and withdrawal of this grounds of objection.

Response to Claim Objections

A. Claims 143, 144, and 150 stand objected for the parenthetical recitation of SEQ ID NO:2 in the claims' preambles. Applicants have removed the parentheses from the pending claims. Accordingly, Applicants submit that the objection has been rendered moot and respectfully request its withdrawal.

B. Claims 143 and 144 stand objected for failing to properly state the substitutions at position 148 in the alternative. Applicants have amended claims 143 and 144 in order to do so. Accordingly, Applicants respectfully assert that the objection has been rendered moot and respectfully request its withdrawal.

C. Claims 143 and 144 stand objected for improperly stating their intended Markush groups. Applicants have amended claims 143 and 144 in order to place the Markush groups in the proper format. Accordingly, Applicants respectfully assert that the objection has been rendered moot and respectfully request its withdrawal.

D. Claim 150 stands objected for improperly reciting the... protein of claim 143, wherein said... protein comprises a substitution at position V163. Applicants have amended claim 150 in order to state, wherein said... protein **further** comprises a substitution at position V163. Accordingly, Applicants respectfully assert that the objection has been rendered moot and respectfully request its withdrawal.

Response to the Rejections Under the Judicially Created Doctrine of Obviousness-type Double Patenting:

A. Applied Standard of Review

The original basis for these maintained rejections was set forth in the Final Rejection mailed May 25, 2005:

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application and those of '176 patent have an overlapping scope.

In response, the Applicants added further elements to the base claims in order to insure that the claimed subject matter was patentably distinct from that claimed in the cited patents. The subsequent Office Action failed to address the substantive changes wrought in the claims by the amendments. Rather, the Final Office Action mailed June 19, 2008 repeatedly opined it was unnecessary to do so in the last paragraphs of page 4:

The subject matter of the patented claims falls within the scope of the claims herein as amended 5 April 2008, and the presence or absence of a recitation of a particular position for modification in a pending claim does not alter the scope of the claims based on the disclosure of the specification.

Both Actions applied an improper standard of review and, accordingly, the effect of the Applicants' substantive amendments to the claims have yet to be properly weighed and a proper rejection presented.

The Applicants note that the proper test for non-obviousness is not whether the claims "contain overlapping/closely related subject matter" as set forth in the Actions. Claims to a new species can be patentable over prior art claims to a genus embracing the species. The MPEP §804 II at p. makes this distinction clear at 800-19, upper right column:

Domination and double patenting should not be confused. They are two separate issues. One patent or application "dominates" a second patent or application when the first patent or application has a broad or generic claim which fully encompasses or reads on an invention defined in a narrower or more specific claim in another patent or application. Domination by itself, i.e., in the absence of statutory or nonstatutory double patenting grounds, cannot support a double patenting rejection. *In re Kaplan*, 789 F.2d 1574, 1577-78, 229 USPQ 678, 681 (Fed. Cir. 1986); and *In re Sarrett*, 327 F.2d

1005, 1014-15, 140 USPQ 474, 482 (CCPA 1964). However, the presence of domination does not preclude double patenting. See, e.g., *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968).

Thus, even if some of the claims of a cited patent would be construed to dominate a pending claim, that domination itself is *not* sufficient to support an obviousness-type double patenting rejection.

B. The proper standard of review

The required approach to assessing nonobviousness in the double patenting context is set forth in the MPEP §804 II B at p. 800-21:

A double patenting rejection of the obviousness-type, if not based on an anticipation rationale, is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. In re Braithwaite, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Therefore, the analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination. In re Braat, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Applicants respectfully point out that recent cases such as *KSR International v. Teleflex, Inc.* (127 S. Ct. 1727) unambiguously affirm the law set forth in *Graham v. John Deere Co.* (86 S.Ct. 684) requiring the Patent Office to determine "[t]he scope and content of the prior art" and compare that content to pending claims. See *KSR*, 127 S. Ct. at 1729-30, and also at 1742 (warning the fact finder to "be aware ... of the distortion caused by hindsight bias and ... cautious of arguments reliant upon *ex post* reasoning"). As set forth in, the *Graham* factors, including the use of objective evidence of secondary considerations to rebut a *prima facie* case of obviousness, as well as, a flexible use of the teaching, suggestion, motivation test remains the framework to be followed for a determination of obviousness in light of *KSR*.

To establish a *prima facie* case of obviousness, three basic criteria must be met:

(1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference must teach or suggest all the claim limitations. MPEP § 2143. See also, *In re*

Rouffet, 47 USPQ2d 1453. The court in *Rouffet* stated that "even when the level of skill in the art is high, the Board must identify specifically the principle, known to one of ordinary skill, that suggests the claimed combination." *Rouffet* at 1459. The court has also stated that actual evidence of a suggestion, or teaching, or motivation to combine is required and the showing of a suggestion, or teaching, or motivation to combine must be "clear and particular." *In re Dembiczak*, 50 USPQ2d 1614, 1617 (1999).

Any obviousness-type double patenting rejection should make clear: (A) The differences between the inventions defined by the conflicting claims – a claim in the patent compared to a claim in the application; and (B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim at issue >is anticipated by, or< would have been an obvious variation of >, < the invention defined in a claim in the patent.

(See, MPEP §804 Rev. 5, Aug. 2006, passage bridging pages at 800-21 -22)

The MPEP then proceeds to caution the Examiner against wholesale use of the prior patents specifications as they are *not* prior art.

i. Response to the rejection of claims 143-146, 148-151, and 188-190 over each of U.S. Patents Nos. 6,150,176 and 6,780,975.

As amended, independent claims 143 and 144 no longer set forth particular mutations at Y66 and Q69 and thus require *additional* mutations which are *not* set forth in any of the claims of the cited patents.

As these prior amendments to the claims set forth subject matter which is patentably distinct from that of each of the cited patents, regardless of any domination thereof, the Applicants respectfully request that these rejections pursuant to the judicially created doctrine of non-obviousness type double patenting be reconsidered and withdrawn.

ii. Response to the rejection of claims 143-146, 148-151, and 188-190 over claims 1-13 and 17-26 of U.S. Patent No. 7,015,310.

Applicants note that the instantly pending claims require a fluorescent protein comprising the amino acid substitutions T203Y; S65G; S72A; V68L; and H148Q or H148G; and at least one substitution selected from the group consisting of R96K; Q183N or K; V150S, T, Q,

N A, C, M, G or L; I152L, V, F, S, T, Q, N A, C, M, or G; F165Y, W, or L; H181F, W, K or R; Q183R, N, S, or C; L201S, T, Q, N, V, I, A, C, M, or G.

In contrast to the instantly pending claims, claims 1 to 13 and 17 to 26 of the '310 patent are drawn to fluorescent proteins having a cysteine at at least two residues selected from positions 147, 149, 202, and 204. Further dependent claims of the '310 patent require that the identity of one or both of residues 48 and 65 be serine and threonine, respectfully.

As none of the claims in the '310 patent recite a *single* specific mutation as required by the instantly pending claims, let alone a particular combination of mutations as set forth in independent claims 143 and 144, Applicants submit that the pending claims are clearly not obvious over claims 1 to 13 and 17 to 26 of U.S. Patent No. 7,015,310. Accordingly, Applicants respectfully request that the above grounds for rejection be reconsidered and withdrawn.

Response to the Rejection Under 35 U.S.C. §112, First Paragraph:

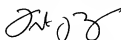
Claims 143 to 146, 148 to 151, and 188 to 190 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly not enabled with respect to the preparation of fluorescent proteins capable of emitting light of wavelengths longer or shorter than the visible spectrum. In an earnest attempt to expedite prosecution, and without acquiescing on the merits of the rejection, Applicants have amended independent claims 143 and 144 in order to set forth an embodiment, wherein said functional engineered fluorescent protein has fluorescent emission in the visible spectrum. Accordingly, in light of the present amendment, Applicants submit that the above grounds for rejection have been fully addressed and respectfully request that they be reconsidered and withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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